

A method for vaccinating a mammal against an antigen, comprising: 1. introducing into the mammal an effective dose of the antigen or an epitope(s) thereof; and

administering to the mammal a topical treatment in an amount sufficient to increase the number of antigen-bearing dendritic cells in a lymphoid organ,

wherein introducing the antigen and administering the treatment are performed independently in any order.

- 2. The method of Claim 1, wherein the topical treatment comprises a lipophilic molecule capable of traversing the stratum corneum and inducing immature dendritic cells to migrate to the draining lymphoid organ.
- 3. The method of Claim 2, wherein the lipophilic molecule is selected from the following formulas:

$$R_3$$
 V
 XR_1
 R_4
 XR_2
 XR_3
 XR_4
 XR_2
 XR_3
 XR_4
 XR_2
 XR_3
 XR_4
 XR_2
 XR_3
 XR_4
 XR_5
 XR_4
 XR_5
 XR_5
 XR_6
 XR_7
 XR_8
 XR_9
 XR_9

wherein R₁ and R₂ are independently alkyl side chains containing 1 to 16 carbon atoms, C_1 to C_{16} substituted alkyl, C_3 to C_{10} cycloalkyl, C_3 to C_{10} substituted cycloalkyl, C_2 to C_{10} alkenyl, C_2 to C_{10} substituted alkenyl, C_2 to C_{10} alkynyl, C_2 to C_{10} substituted alkynyl;

wherein R₃, R₃', R₄ and R₄' are selected independently from the group consisting of hydrogen atom, hydroxy group, halogeno group, alkyl side chains containing 1 to 16 carbon atoms, C₁ to C₁₆ substituted alkyl, C₃ to C₁₀ cycloalkyl, C₃ to C_{10} substituted cycloalkyl, C_2 to C_{10} alkenyl, C_2 to C_{10} substituted alkenyl, C_2 to C_{10} alkynyl, C₂ to C₁₀ substituted alkynyl, C₇ to C₁₆ phenylalkyl, C₇ to C₁₆ substituted phenylalkyl, phenyl, substituted phenyl, naphthyl and substituted naphthyl;

wherein X is an oxygen or a nitrogen atom; and

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wherein W is a saturated or unsaturated chain consisting of C_1 - C_{10} alkyl, C_1 - C_{10} substituted alkyl, C_1 - C_{10} phenylalkyl, C_7 - C_{16} substituted phenylalkyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, C_3 - C_7 cycloalkyl and C_3 - C_7 substituted cycloalkyl group, and wherein each terminus of the chain is bonded to the carbon $C(R_3R_3)$ and $C(R_4R_4)$.

- 4. The method of Claim 3, wherein W contains one or more heteroatoms selected from the group consisting of nitrogen, sulfur, and oxygen in combination or independently.
- 5. The method of Claim 3, wherein the R_1 and R_2 groups are identical C_1 to C_6 alkyl moieties.
 - 6. The method of Claim β , wherein R_1 and R_2 are $(CH_2)_3$ - CH_3 .
- 7. The method of Claim 3, wherein X is an oxygen and R_3 and R_4 are linked to form a ring structure which, including the W chain, comprises a saturated or unsaturated C_3 to C_{10} cycloalkyl, C_3 to C_{10} substituted cycloalkyl, C_7 to C_{16} phenylalkyl, C_7 to C_{16} substituted phenylalkyl, phenyl, substituted phenyl, naphthyl or substituted naphthyl.
 - 8. The method of Claim 7, wherein the ring structure is an aryl group.
- 9. The method of Claim 7, wherein the ring structure contains one or more heteroatoms selected from the group consisting of nitrogen, sulfur, and oxygen.
- 10. The method of Claim 3, wherein the lipophilic molecule comprises a terpene.
- 11. The method of Claim 2, wherein the lipophilic molecule is selected from the group consisting of dibutyl phthalate, dibutyl-D-tartarate, N,N-diethyl-toluamide, dibutylfumarate, di(2-ethylhexyl)fumarate, diisooctylmaleate, diethylhexylmaleate, diisooctylfumarate, benzoic acid, bihenylmaleate, dioctylphthalate, dibutylmaleate, dioctylmaleate, dibutylsuccinate, dioctylsuccinate, dinonylphthalate, diisononylphthalate, dimethylphthalate, diethylphthalate, dipropylphthalate, diphenylphthalate, dibenzylbutylphthalate, diethylmethylphthalate and camphor.
 - 12. The method of Claim 2, wherein the lipophilic molecule is ≤500 daltons.
- 13. The method of Claim 2, wherein the lipophilic molecule has an oil/water partition coefficient >1.

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- 14. The method of Claim 13, wherein the lipophilic molecule has an oil/water partition coefficient of between about 10 and about 10⁶.
- 15. The method of Claim 2, wherein the topical treatment further comprises an organic solvent.
 - 16. The method of Claim 15, wherein the organic solvent is acetone.
- 17. The method of Claim 1, wherein the topical treatment comprises application of ultrasound energy.
- 18. The method of Claim 1, wherein the antigen or epitope(s) thereof is introduced into the mammal by a virus, a bacterium, a fungus, or a parasite.
- 19. The method of Claim 1, wherein the antigen or epitope(s) thereof is introduced into the mammal by ingestion.
- 20. The method of Claim 1, wherein the antigen or epitope(s) thereof is introduced into the mammal by disrupting the stratum corneum.
- 21. The method of Claim 1, wherein the antigen or epitope(s) thereof is introduced into the mammal by injection.
- 22. The method of Claim 21, wherein the injection is made via a route selected from the group consisting of intraepidermal, intradermal, subcutaneous, intramuscular, intravascular, or into a specific organ.
- 23. The method of Claim 1, wherein the antigen or epitope(s) thereof is introduced into the mammal via delivery to at least a portion of the respiratory, urogenital or gastrointestinal tracts.
- 24. The method of Claim 1, wherein the antigen or epitope(s) thereof is introduced into the mammal by a transfer of cells containing the antigen or epitope(s) thereof.
- 25. The method of Claim 1, wherein the antigen or epitope(s) thereof is introduced into the mammal by transformation of a cell within the mammal and expression of the antigen or epitope(s) thereof by the transformed cell.
- 26. The method of Claim 25, wherein the transformation is induced by the transfer of a nucleic acid encoding the antigen or epitope(s) thereof.
- 27. The method of Claim 1, wherein the antigen or epitope(s) thereof is endogenous to the mammal and is either normal or pathologic.

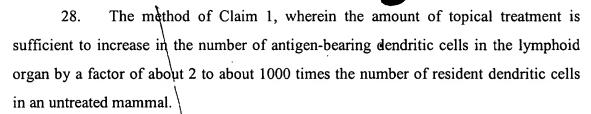
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29. The method of Claim 28, wherein the number of antigen-bearing dendritic cells in the lymphoid organ is increased by a factor of about 5 to about 100 times the number of resident/dendritic cells in an untreated mammal.

30. The method of Claim 1, wherein the amount of topical treatment is further characterized as being sufficient to increase local release of an endogenous inducer of dendritic cell migration and maturation.

31. The method of Claim 1, wherein the amount of topical treatment is further characterized as being sufficient to alter the plasma membrane expression or function of an adhesion molecule.

32. A method of immunication against an antigen in a mammal, comprising: introducing into the mammal an expression vector adapted to induce the prolonged expression of the antigen on epitope thereof; and

administering a topical treatment to the mammal during a period when the antigen is being expressed, wherein the topical treatment is administered in an amount sufficient to increase the number of antigen-bearing dendritic cells in a draining lymphoid organ.

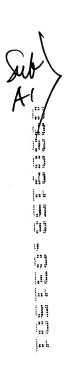
- 33. The method of Claim 32 wherein the antigen or epitope(s) thereof is endogenous to the mammal.
- 34. The method of Claim 32 wherein the topical treatment is administered repeatedly at periodic intervals during the period when the antigen is being expressed.
- 35. The method of Claim 32, wherein the topical treatment comprises a lipophilic molecule capable of traversing the stratum corneum and inducing immature dendritic cells to migrate to the draining lymphoid organ.
- 36. The method of Claim 35, wherein the lipophilic molecule is selected from the following formulas:

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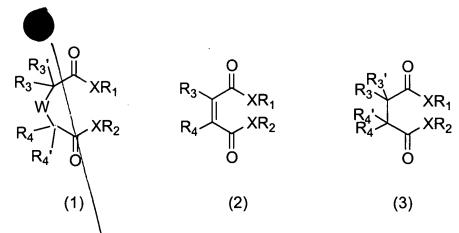
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wherein R_1 and R_2 are independently alkyl side chains containing 1 to 16 carbon atoms, C_1 to C_{16} substituted alkyl, C_3 to C_{10} cycloalkyl, C_3 to C_{10} substituted cycloalkyl, C_2 to C_{10} alkeryl, C_2 to C_{10} substituted alkynyl;

wherein R_3 , R_3 , R_4 and R_4 , are selected independently from the group consisting of hydrogen atom, hydroxy group, halogeno group, alkyl side chains containing 1 to 16 carbon atoms, C_1 to C_{16} substituted alkyl, C_3 to C_{10} cycloalkyl, C_3 to C_{10} substituted cycloalkyl, C_2 to C_{10} alkenyl, C_2 to C_{10} substituted alkenyl, C_2 to C_{10} substituted alkynyl, C_2 to C_{10} substituted phenylalkyl, phenyl, substituted phenyl, naphthyl and substituted naphthyl;

wherein X is an oxygen or a nitrogen atom; and

wherein W is a saturated or unsaturated chain consisting of C_1 - C_{10} alkyl, C_1 - C_{10} substituted alkyl, C_7 - C_{10} phenylalkyl, C_7 - C_{16} substituted phenylalkyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, C_3 - C_7 cycloalkyl and C_3 - C_7 substituted cycloalkyl group, and wherein each terminus of the chain is bonded to the carbon $C(R_3R_3)$ and $C(R_4R_4)$.

- 37. The method of Claim 36, wherein W contains one or more heteroatoms selected from the group consisting of nitrogen, sulfur, and oxygen in combination or independently.
- 38. The method of Claim 36, wherein the R_1 and R_2 groups are identical C_1 to C_6 alkyl moieties.
 - 39. The method of Claim 36, wherein R_1 and R_2 are $(CH_2)_3$ - CH_3 .
- 40. The method of Claim 36, wherein X is an oxygen and R₃ and R₄ are linked to form a ring structure which, including the W chain, comprises a saturated or

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unsaturated C₃ to C₁₀ cycloalkyl, C₃ to C₁₀ substituted cycloalkyl, C₇ to C₁₆ phenylalkyl, C₇ to C₁₆ substituted phenylalkyl, phenyl, substituted phenyl, naphthyl or substituted naphthyl.

- The method of Claim 36, wherein the ring structure is an aryl group. 41.
- 42. The method of Claim 36, wherein the ring structure contains one or more heteroatoms selected from the group consisting of nitrogen, sulfur, and oxygen.
- 43. The method of Claim 35, wherein the lipophilic molecule comprises a terpene.
- The method of Claim 35, wherein the lipophilic molecule is selected 44. from the group consisting of dibutyl phthalate, dibutyl-D-tartarate, N,N-diethyltoluamide, dibutylfumarate. di(2-ethylhexyl)fumarate, diisooctylmaleate, diethylhexylmaleate, diisooctylfumarate, benzoic acid, bihenylmaleate, dioctylphthalate, dibutylmaleate, dioctymaleate, dibutylsuccinate, dioctylsuccinate, dinonylphthalate, dimethylphthalate, diisononylphthalate, diethylphthalate, dipropylphthalate, diphenylphthalate, dibenzylbutylphthalate, diethylmethylphthalate and camphor.
- 45. The method of Claim 35, wherein the lipophilic molecule is ≤500 daltons.
- 46. The method of Claim 35,\wherein the lipophilic molecule has an oil/water partition coefficient >1.
- The method of Claim 46, wherein the lipophilic molecule has an 47. oil/water partition coefficient of between about 10°.
- The method of Claim 35, wherein the topical treatment further comprises 48. an organic solvent.
 - The method of Claim 48, wherein the organic solvent is acetone. 49.
- 50. The method of Claim 32, wherein the topical treatment comprises application of ultrasound energy.
- A method for vaccinating a mammal against an antigen, comprising: 51. injecting into the mammal an effective dose of the antigen or an epitope(s) thereof; and
- administering to the mammal a topical treatment in an amount sufficient to increase the number of antigen-bearing dendritic cells in a draining lymphoid organ,

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wherein the topical treatment comprises a lipophilic molecule with a molecular weight of ≤500 daltons.

- 52. A method for enhancing an immune response in a mammal against an endogenous antigen, comprising repeated topical application to the mammal of a lipophilic compound having a molecular weight ≤500 daltons, wherein the lipophilic compound is applied in an amount sufficient to increase the number of antigen-bearing dendritic cells in a lymphoid organ.
- 53. The method of Claim 52, wherein said endogenous antigen is a tumor antigen.

54. A method for vaccinating a mammal against an antigen, comprising:

delivering to the mammal a nucleic acid vaccine, comprising DNA or

RNA encoding the antigen or an epitope(s) thereof; and

administering to the mammal a topical treatment in an amount sufficient to increase the number of antigen-bearing dendritic cells in a lymphoid organ,

wherein the topical treatment comprises a lipophilic molecule with a molecular weight of ≤500 daltons.

55. A method for vaccinating a mammal against an antigen, comprising:

providing the mammal with an effective dose of the antigen or an epitope(s) thereof; and

administering internally to the mammal a treatment in an amount sufficient to increase the number of antigen-bearing dendritic cells in a lymphoid organ.

- 56. The method of Claim 55, wherein administering the treatment internally occurs via a route selected from the group consisting of injection, delivery into an organ, and delivery to the gastrointestinal, respiratory or urogenital tracts.
- 57. The method of Claim 55, wherein the treatment comprises a lipophilic molecule with a molecular weight of ≤500 daltons or low frequency ultrasound energy.

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